

IN THE US PATENT AND TRADEMARK OFFICE

In re application of

Ezio BOMBARDELLI

Serial No. 10/563,965

Group Art Unit 1614

Filed: *January 10, 2006*

Examiner: *Qiuwen, Mi*

For: "*COMBINATIONS OF VASOACTIVE AGENTS, THEIR USE IN THE PHARMACEUTICAL AND COSMETIC FIELD, AND FORMULATIONS CONTAINING THEM*"

DECLARATION UNDER RULE 132

I, Ezio Bombardelli, declare and state as follows

1. I am citizen of Italy, residing at Pavia (Italy), Via Gabetta, 13.
2. I am inventor of the invention described and claimed in the above-identified patent application.
3. I received a degree in Biological Science from the University of Pavia in 1962. From 1962 to 1989 I was a researcher, then I held the position of Head of the Research Laboratory at the company "Inverni della Beffa S.p.A." – Milan. Since 1986, I have been Scientific Director of INDENA S.p.A., Milan. I am the author of more than 80 scientific publications, most of which concern medicinal plant technology. I am the inventor or co-inventor in more than thirty patents all concerning medicinal plant derivatives. I am a member of the Italian Chemical Society, Fédération Internationale Pharmaceutique (F.I.P.), Gesellschaft für Arzneipflanzenforschung and Phytochemical Society of Europe.
4. The experimental activities reported hereafter have been carried out under my supervision and responsibility:

Comparative test

The following gel formulation has been prepared in accordance with the above-referenced patent application:

Test composition (gel)

Visnadin	0.30 g
Ginkgo biloba dimeric flavones complexed with phospholipids	0.40 g
Escin beta-sitosterol complexed with phospholipids	1.00 g
Lecithin	15.00 g
Cholesterol	0.50 g
Ethanol	8.00 g
Butylhydroxy toluene	0.01 g
Imidazolidine urea	0.30 g
Hydroxypropyl-methylcellulose	2.00 g
Water	qs 100.00 g

The effect of the test composition was evaluated on 10 women suffering from cellulite, aged between 25 and 36 and weighing 63.6 ± 2.9 kg on average. For comparison, 4 groups of 10 women each were treated with a placebo and with three different formulations, respectively, each of them containing one of the active ingredients present in the test composition and the same excipients, according to the following scheme:

Group	Active ingredient	Concentration
1 (placebo)	-	-
2	Visnadin	0.3%
3	Ginkgo biloba dimeric flavones complexed with phospholipids	0.4%
4	Escin beta-sitosterol	1.0%

	complexed with phospholipids	
5 (test composition)	- Visnadin	0.3%
	- Ginkgo biloba dimeric flavones complexed with phospholipids	0.4%
	- Escin beta-sitosterol complexed with phospholipids	1.0%

Each woman was treated topically on the thighs with 1g formulation twice a day for 45 consecutive days. Four hours after the last treatment, the skin macrorelief ("orange peel effect") was measured with the "*profilometry on digital imaging of pinched thighs analysis*" according to Bertin C. et al. J. Cosmet. Sci., 52, 199-210, 2001. In addition, the thigh circumference was measured according to Gasbarro V. and Vettorello G. F. in Cosmetics and Toiletries, 107, 64-66, 1992.

The results reported in Tables 1 and 2 below show that the effect of the test composition is higher than the sum of the effects of the placebo and of the formulations containing a single active ingredient.

Table 1 – Effect of the tested formulations on profilometric analysis of thigh macrorelief (Rz)

Group	T ₀	T ₄₅
1	7.33 ± 0.6	7.30 ± 0.2
2	7.22 ± 0.7	6.38 ± 0.3
3	7.31 ± 0.3	6.52 ± 0.4
4	7.15 ± 0.4	6.12 ± 0.7
5	7.24 ± 0.3	3.65 ± 0.3**

Rz = roughness parameter

** < 0.001 vs basal, Student's t test

Table 2 – Effect of the tested formulations on left thigh circumference (cm)

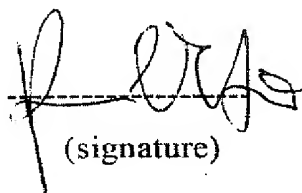
Group	T ₀	T ₄₅
1	57.3 ± 0.1	57.0 ± 0.2
2	57.7 ± 0.2	57.6 ± 0.1
3	59.2 ± 0.2	57.7 ± 0.1
4	54.5 ± 0.2	54.2 ± 0.1
5	56.4 ± 0.1	53.2 ± 0.1*

* < 0.05 vs basal, Student's t test

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

July 18, 2008

(date)


(signature)